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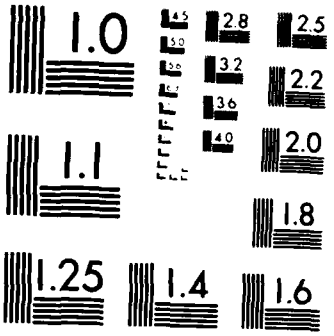

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# Army Drug Development Program
# Phase I
# Clinical Testing

## FINAL REPORT

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April 1985

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

Contract No. DAMD17-83-C-3001

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The research performed by BIO-MED, Inc. under contract DAMD17-83-3001 was in support of experiments as directed by the COTR and Director, Experimental Theraputics, WRAIR. DAMD17-83-C-3001 was a continuation of contract DAMD17-75-C-5036 prior to its termination at the convenience of the government. During the eight months the contract existed, in collaboration with WRAIR, eight reports were completed.

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## SUMMARY

This is the final report of DAMD17-83-C-3001 under which BIO-MED, Inc. performed clinical pharmacologic studies.

The subject contract was a successor to DAMD-17-75-C-5036 (15 Feb. 1975 to 18 August 1983). BIO-MED, Inc. continued to apply the same policies, procedures and operational activities under 3001 that had been developed during the preceding eight and one-half years under contract 5036. However, contract 3001 was terminated 30 April, 1984 at the convenience at the government for reasons not stated and not clear to BIO-MED, Inc.

During the interval from 19 August 1983 to 30 April, 1984, BIO-MED, Inc. was involved in the following activities under terms of the contract:

1. Consultation with the Division of Experimental Therapeutics at the Walter Reed Army Institute of Research (WRAIR) regarding drugs under development and the anticipated requirment for Phase I Clinical Studies.

2. The development of protocols for Phase I Clinical Studies and the administrative and technical processing of these protocols including (a) appropriate scientific consultation regarding medical aspects of the studies, (b) institutional review including review of the protocol by a duly constituted Institutional Review Board, and (c) submission of the protocol(s) to the sponsoring agency for their internal review mechanisms and the incorporation of modifications indicated by such reviews.

3. The implementation of protocols which included subject recruitment, identification and medical qualification; the provision for the clinical environment for the conduct of the study including nursing, dietetic, laboratory and custodial services; the conduct of the study including the immediate medical supervision of drug administration, subject evaluation and specimen collection; the timely analysis of prescribed procedures such as ECGs, roentgenograms and the medical follow-up of each subject until his eventual separation from the study.

4. Analysis, interpretation and reporting of the results of studies.

5. Provision of space and technical support to Division of Experimental Therapeutics, WRAIR for establishment of on site valid assays of acetylcholinesterase needed for clinical studies of pyridostygmine including administration to human subjects. A valid reproducible acetylcholinesterase assay

activity in human biologic fluids is considered an absolute necessity prior to experimental administration of the drug to normal human subjects.

This report is a final compilation of the studies conducted under this research contract.

## FOREWORD

BIO-MED, Inc. is a privately held medical research organization, incorporated in the District of Columbia and registered in the state of Maryland.

Contract DAMD17-83-C-3001 became effective August 19, 1983. That contract stipulated that:

"The objective of the contract is to carry out Phase I clinical pharmacology studies (safety, tolerance and/or pharmacokinetics) in humans. These studies will support the U.S. Army Drug Development Program." (DAMD17-82-Q-0003).

BIO-MED, Inc. commenced these studies 19 August, 1983. On 30 April, 1984, this contract was terminated at the convenience of the government.

During the reporting period, this organization has been engaged in studies of safety, tolerance and pharmacokinetics of drugs developed by or of interest to the Army Drug Development Program.

For the protection of human subjects the investigators have adhered to policies of applicable Federal Law 45CFR46.

## FINAL REPORT

DAMD17-83-C-3001 was awarded to BIO-MED, Inc. as a successor contract to DAMD-17-75-5306 for the purpose of continuing Phase I Clinical Testing of drugs critical to the military mission under the guidance of the Division of Experimental Therapeutics, WRAIR. BIO-MED, Inc. participation in the military mission had been continuous since the award of contract 5036 in February 1975 to termination of contract 3001 at the convenience of the government 30 April, 1984. During the term of the contract 19 August 1983 to 30 April 1984 and continuing BIO-MED, Inc. activities for the closing out of the contract, the following has been accomplished:

1. Revisions were made to the protocol "Phase I Safety and Tolerance Testing for the Pediculicide, ABATE: Cutaneous Toxicity and Sensitivity." This protocol was developed and received IRB approval during the term of the previous contract. The protocol received HSRRB approval during the term of the subject contract.

2. The protocol, "Pharmacokinetics of WR 6026 2HCL", was prepared and received IRB and HSRRB approval. Part I of the protocol was implemented and completed (2 April - 7 April 1984). Two subjects were enrolled in the study.

3. The protocol, "Pharmacokinetics and Bioavailability of WR 194,965 Following a Single Oral Dose", was prepared and received IRB and HSRRB approval. Part I of the protocol was implemented and completed (6 February - 6 March 1984). Four subjects were enrolled in the study.

4. The protocol, "Pharmacokinetics of Orally Administered Pyridostigmine and Comparative Bioavailability of the Liquid and Tablet Formulation at the 60 mg Dose Level", was prepared and received IRB approval. The protocol also received HSRRB approval, with certain provisions, which have since been incorporated into the protocol.

5. In cooperation with the Division of Experimental Therapeutics, WRAIR, experimental whole blood, plasma and RBC acetylcholinesterase assays have been conducted at the BIO-MED, Inc. clinical facility. BIO-MED has provided blood donors and facilities for these experiments.

6. Complete medical evaluations (screening) of 34 applicants for participation as study subjects were performed.

7. Two quarterly reports of activities accomplished during the subject contract term have been submitted to WRAIR.

8. The following reports of activities accomplished under the previous contract were prepared during the term of the subject contract:

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| Annual report 1979 | distributed |
| Annual report 1980 | draft submitted (USAMRDC) |
| Annual report 1981 | draft submitted " |
| Annual report 1982 | draft submitted " |
| Annual report 1983 | in preparation |
| Final report 1975 - 1983 | draft submitted (USAMRDC) |
| Final clinical report Experiment #21 (WR 6026) | draft submitted (WRAIR) |
| Final clinical report Experiment #22 (Diet Study) | in preparation |
| Final clinical report Experiment #23 (WR 194,965) | in preparation |

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MARCH, 1988

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